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Diagnosis and interpretation of testing for cat scratch disease

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ABSTRACT

Cat scratch disease (CSD) is an infectious disease caused by *Bartonella henselae* that presents as regional lymphadenopathy which can appear within weeks after a cat scratch. There is no gold standard for diagnosis. Rather, clinicians rely on an amalgam of criteria to make a definitive diagnosis. We describe a case of a 44-year-old woman with six cats who presented with a painful left inguinal mass, had splenic lesions on imaging, and had positive serology but a negative polymerase chain reaction test for *B. henselae*.

KEYWORDS *Bartonella henselae*; cat scratch disease; polymerase chain reaction

Cat scratch disease (CSD) is an infectious disease caused by *Bartonella henselae*. Patients may present with regional lymphadenopathy, fever, erythema, or ocular involvement. It is rare and typically self-limiting; however, there is a potential for dissemination to vital organs. There is no gold standard for diagnosis. Clinicians rely on a variety of diagnostic tests and a high clinical suspicion for the disease based on presentation. Thus, it is important to understand how to interpret tests accurately to diagnose patients in a timely manner. We present a case of a 44-year-old woman diagnosed with CSD who had a positive antibody titer but a negative polymerase chain reaction (PCR) test.

CASE DESCRIPTION

A 44-year-old woman with a remote and untreated positive PPD test presented with a painful and progressively enlarging left groin mass. She was afebrile and endorsed nausea, vomiting, and a 9-pound weight loss over the past 2 months. A computed tomography (CT) scan showed hepatosplenomegaly with numerous splenic hypodensities and an enlarged left inguinal lymph node with surrounding inflammation *(Figure 1)*. A chest x-ray and a QuantiFERON-TB Gold blood test were negative for tuberculosis. The patient worked in food services and denied recent travel and sick contacts.

Testing for viral hepatitis, HIV, human papillomavirus, chlamydia, gonorrhea, COVID-19, histoplasmosis, cryptococcosis, brucellosis, and coccidioidosis was unrevealing, as were blood and urine cultures. Core biopsy of the left inguinal node showed granulomatous inflammation with no acid-fast or fungal organisms. Cytopathology was negative for malignancy. Upon further questioning, the patient revealed she had six cats, including two kittens, and had been scratched in recent weeks. There was strong suspicion for CSD so the patient was transitioned from empiric ceftriaxone and metronidazole to azithromycin. Lab tests demonstrated an elevated *B. henselae* IgG antibody titer at 1:1280. *B. henselae* IgM and *B. quintana* IgG and IgM were negative. Paraffin-embedded lymph node tissue was sent for PCR analysis. Given the high likelihood of CSD and symptomatic improvement with antibiotics, the patient was discharged to complete 5 days of azithromycin, the standard therapy recommended by the Infectious Diseases Society of America, with the *Bartonella* PCR tissue sample still pending.

Two days later, the patient returned with persistent fever, left upper quadrant pain, and swelling of the left inguinal lymph nodes despite compliance with azithromycin. Repeat imaging was unchanged. Interestingly, results of the PCR analysis from the initial tissue sample were negative for *B. henselae* and *B. quintana*. However, given the patient's history of cat scratches, clinical presentation, and positive serology, CSD remained the primary diagnosis. At this point,

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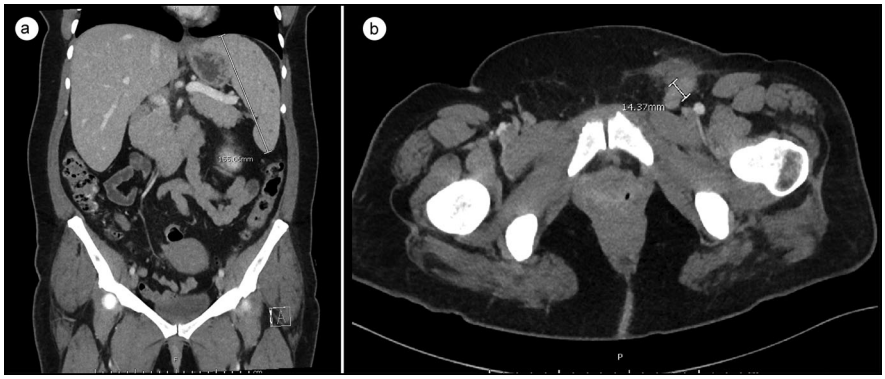

Figure 1. **(a)** Coronal image of the abdomen and pelvis demonstrating splenomegaly with numerous small splenic hypodensities, which in conjunction with clinical presentation is compatible with disseminated cat scratch disease. **(b)** Axial image of the pelvis showing an enlarged left inguinal lymph node with adjacent inflammatory fat stranding.

the infectious disease team opted to treat the patient with 14 days of both rifampin and azithromycin. The patient showed improvement of symptoms upon discharge.

DISCUSSION

This case report describes the unique presentation of a patient with high clinical suspicion for CSD with a positive antibody titer and a negative PCR. CSD is caused by *B. henselae*, and it presents with regional lymphadenopathy appearing 1 to 7 weeks after a cat scratch.[1] The incidence is about 10 cases per 100,000 people per year in the US, with peaks in January, summer, and fall.[2,3] While uncomplicated lymphadenopathy typically resolves spontaneously,[4] early diagnosis and treatment is important, as there is potential for dissemination to the liver, spleen, bone, and heart causing culture-negative endocarditis.

There is no gold standard to diagnose *B. henselae* in CSD. Thus, clinicians rely on several criteria for definitive diagnosis, which include a history of contact with cats, histology showing granulomas, and a positive serology with immunofluorescence assay for antibodies against *B. henselae*.[1,3] Serological testing for *B. henselae* antibodies, the first microbiological test available,[3] is often used since other methods may require specific equipment.[4] It is well documented that IgG titers >1:256 are diagnostic, with studies showing variability in sensitivity and specificity.[2,5,6] Because of this variability, there has been an increase in use of concurrent PCR as a diagnostic tool. One study showed that for patients definitively diagnosed with CSD, PCR results had a sensitivity of 76% while specificity was 100%.[1] PCR for paraffin-embedded lymph nodes, as in our patient, has shown lower sensitivities of 40% to 70%.[1]

Based on these studies, a negative PCR result does not exclude a patient from a CSD diagnosis. Rather, there are multiple aspects that impact PCR results. False-negatives may be explained by the lack of sensitivity, timing of tissue biopsy, samples taken after long periods of antibiotic therapy, or the presence of other *Bartonella* species.[1,7] One study showed that PCR was only positive in lymph nodes biopsied within 6 weeks of illness.[7] In our patient, with long-standing cat exposure, the duration of illness may have exceeded 6 weeks. Thus, PCR results may be negative for patients with true CSD, as is likely the case for our patient.

Ultimately, there is no sole criterion for diagnosis of CSD. When a patient has a negative PCR result, diagnosis may rely on exclusion of other causes of lymphadenopathy and having at least two of the following: (1) positive *Bartonella* serology, (2) positive histology showing granulomas, and (3) contact with cats.[1] While our patient had a negative PCR, she was positive for the other criteria. As clinicians, it is important for us to understand the sensitivity and specificity of diagnostic testing in order to interpret results accurately and treat patients appropriately. This case report demonstrates the importance of holistically diagnosing a patient presenting with CSD with a thorough history, physical exam, and correct interpretation of laboratory testing.

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